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EXAMINER	
LEAVITT, MARIA GOMEZ	
ART UNIT	PAPER NUMBER
1633	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/571,277	OKANO ET AL.	
	Examiner	Art Unit	
	MARIA LEAVITT	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *1-17, 20, 23-26 and 28-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,19,21,22,27 and 31-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Applicants' amendment filed on 10-14-2008 has been entered.
3. Status of claims. Claims 1-41 are pending. Claims 21, 27 and 34 have been amended and claims 38-41 have been added by Applicants' amendment filed on 10-14-2008. Claims 1-17, 20, 23-26 and 28-30 were previously withdrawn from consideration as being directed to non-elected inventions pursuant to 37 CFR1.14(b), there being no allowable generic or linking claim. Applicants' election of species Galectin-1 in the reply filed on 11-15-2007 was previously acknowledged. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
4. Therefore claims 18, 19, 21, 22, 27, 31-41 are currently being examined to which the following grounds of rejection are applicable.

Response to arguments

Withdrawn objection/ rejections in response to Applicant arguments or amendments:

Specification objection

In view of Applicants' amendment of the specification at page 3, lines 6-18, to correct the spelling of the term "Galectin-1", objection to the specification has been withdrawn.

In view of Applicants' amendment of the specification at page 15, line 23 bridging to page 16, line 4, objection to the specification has been withdrawn.

In view of Applicants' arguments alleging support for the contention that a population of SVZ astrocytes functioning as stem cells ultimately differentiate into neuroblasts, objection to the specification at page 22, lines 24-25, has been withdrawn.

Claim Objection

In view of Applicants' amendment of claim 21 to spell out the terms "SVZ" and of claims 27 and 34 to spell out the abbreviation "C-S", objection to the claims has been withdrawn.

Rejection maintained in response to Applicants' arguments or amendments.

Claim Rejections - 35 USC § 103

Claims 18, 19, 27 and 31- 35 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Horie et al., (US Patent 6,890,531, Date of Issue May 10, 2005) in view of Well et al., (Cell, 1991, pp. 91-97) for the reasons of already of record set forth in the Office action of 05-14-2008, and the reasons set forth in the following paragraph.

Horie discloses mutant Galactin-1 polypeptide in which a cys at position 2 was converted to ser (col. 38, lines 35-38; col. 39, lines 15-19) (Current **claims 27 and 34, in part**). Moreover, Horie discloses that Galectin is a generic name for an animal lectin, and is also called β galactoside-binding animal lectin or S-type lectin (col. 1, lines 40-42).

Response to Applicants' Arguments as they apply to rejection of claims 18, 19, 27 and 31- 35 under 35 USC § 103

At page 5 of remarks, Applicants essentially argue that Horie identified Galectin-1 as a nerve-regeneration-promoting factor. Moreover, Applicants contend that the only experiments disclosed in Horie addressing the effects of Galectin-1 are on nerve injury or nerve regeneration on the sciatic nerve (Examples 18 and 19). In addition, Applicants allege that there is no teaching in Horie to associated neuronal stem cells with the sciatic nerve. Furthermore, applicants assert that the phenomenon of nerve regeneration in a peripheral never (e.g., sciatic nerve) is completely different from the proliferation of neuronal stem cells. Such is not persuasive.

As stated in the previous office action filed on 05-14-2008, the only active step placed on the method of independent claims 18, 21, 31 and 36 is the administration of Galectin-1 to the brain. The recitation of the intended used in the claimed invention, namely, proliferation of neuronal stem cells in the preamble of claims 18, 21, 32, and 36 fails to impart any physical or structural property to the method of administration. In contrast to applicants' assertions, Horie et al., in addition to treatment of the sciatic nerve, teaches treatment of neuropathies of **central nerves** caused by nerve injuries e.g., ischemia, infection, malignant tumor or metabolic disorder or degeneration of specific nerve system cells e.g., amyotrophic lateral sclerosis, diabetic neuropathy, dementia senilis, Alzheimer's disease, Parkinson's disease and the like are intractable (col. 2, lines 14-24; col. 13, lines 6-29), wherein administration of galectin-1, contained in collagen, for example, is directly imbedded into the neurological location for treatment (col. 11, lines 60-61). While Horie is silent as to cell proliferation induced by galectin-1 on neuronal stem cells on central nerve injury, administration of galectin-1 to central nerves must have inherently induced neuronal stem cells proliferation, since Horie has performed the same step of the claimed method, i.e., administration of galectin-1 to the brain. Note that the central nerve system

includes the spinal cord level and brain level. Also note that case law states that anticipation does not require the actual creation or reduction to practice of the prior art subject matter; anticipation requires only an enabling disclosure. In re Donohue, 766 F.2d 531, 533 [226 USPQ 619] (Fed. Cir. 1985). A reference may enable one of skill in the art to make and use a compound even if the author or inventor did not actually make or reduce to practice that subject matter. Bristol-Myers, 246 F.3d at 1379; see also In re Donohue, 766 F.2d at 533.

In relation to the teachings of Wells, Applicants essentially argue that Wells does not complements the teachings of Horie as Wells teaches the functionality of the mouse β-galactosidase –binding protein (mGBP) on fibroblasts. Moreover, Applicants allege that in contrast to the claimed invention, mGBP is a negative regulator of proliferation. Such is not persuasive.

As stated in the paragraph above, the only active step placed on the method of independent claims 18, 21, 31 and 36 is the administration of Galectin-1 to the brain. The recitation of the intended used in the claimed invention, namely, proliferation of neuronal stem cells in the preamble of claims 18, 21, 32, and 36 fails to impart any physical or structural property to the method of administration. Wells merely complements the teachings of Horie by disclosing that murine β-galactosidase –binding protein (mGBP) e.g., Galectin, is constitutively associated with cell growth and cell replication. If the steps in the method taught by Wells were to be compared with the only claimed step of the instant invention, one of ordinary skill in the art would not had expected the modulation of cell growth and cell replication in the method taught by Wells to be necessarily of enhanced cell proliferation. Wells results exhibiting inhibition of cell replication and cell arrest of embryonic fibroblasts involve extraction and purification of

mGBP, different cell culture conditions and *in vitro* administration of mGBP at specific concentrations that were well above those required for effector molecules (p. 91, col. 2, last paragraph; p. 95, col. 2, last paragraph). The steps in the method of Wells are not the same as the one claimed in the instant invention. The differences in the type of cultured cell use, source and dose of Galectin-1 used, and evaluation of results make any direct comparison of the data from the two studies (Horie and Wells) inappropriate. Indeed, post filing art of Vas et al., further corroborates how different concentrations of Galectin-1 result in opposing physiological regulation of cell growth and proliferation. Vas et al., teaches that *in vitro* administration of Galecin-1 is biphasic inducing proliferation and survival of murine and human hematopoietic stem at low concentrations whereas inhibiting cell growth and proliferation at high concentrations (Stem Cells. 2005 pp. 279-87). Accordingly, the steps in the method taught by Wells and the method of the claimed invention differ to such extent that the resulting effects on cell growth and cell replication cannot be expected to be the same.

Claims 21, 22, 36 and 37 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Horie et al., (US Patent 6,890,531, Date of Patent May 10, 2005) in view of Well et al., (Cell, 1991, pp. 91-97) as applied to claims 18, 19, 27, 31-34 and 35 above and further in view of Gage et al., US Patent No. 6,436,389 (Date of Issue August 20, 2002) or Taupin et al., (Neuron, 2000, pp. 385-397).

Response to Applicants' Arguments as they apply to rejection of claims 21, 22, 36 and 37 under 35 USC § 103

At pages 14-16 of remarks, Applicants essentially allege that Gage and Taupin do not complement the teachings of Horie and Wells because Gage and Taupin don't mention Galectin-1; therefore, the disclosure of Gage and Taupin cannot remedy the shortcomings of Horie and Wells. Such is not persuasive.

As stated in the previous office action of 05-14-2008, the only active step placed on the method of independent claims 18, 21, 31 and 36 is the administration of Galectin-1 to the brain . The recitation of the intended used in the claimed invention, namely, proliferation of neuronal stem cells in the preamble of claims 18, 21, 32, and 36 fails to impart any physical or structural property to the method of administration. Gage et al., discloses methods for the treatment of neurodegenerative disorders including neural degenerative diseases and cerebral ischemia comprising stereotaxically injection into the rat hippocampus of genetically modified adult hippocampus-derived neuronal progenitor cells (AHPs) to stimulate neurogenesis in the adult rat subventricular zone (SVZ) in the brain. Similarly, Taupin teaches neuronal stem/progenitor cells division in the SVZ after stereotaxically injection into the rat hippocampus of genetically modified AHPs. Hence the combined disclosures of Gage and Taupin complement the teachings of Horie and Wells in relation to the obviousness for one of ordinary skill in the art to have induced proliferation of SVZ astrocytes by administration of Galectin-1 to the brain as this cell population displays neurogenic properties.

New grounds of rejection

Claim Rejections - 35 USC § 103

To the extent that new claims 38-41 read on administration of Galecting-1 to the lateral ventricule of the brain, e.g., specific brain location in the central nerve system, the following rejection applies.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The instant claims are broadly drawn to a method for enhancing *in vivo* proliferation of a neuronal stem cell comprising administration of Galectin-1. The claimed method encompasses solely one active step, i.e., administering Galectin-1. Moreover, the specification does not define the term proliferation; hence the term can broadly be interpreted as one cell that replicates into two. Additionally, the specification is silent about any effective treatment of a neurological disorder. Note that treatment of neurological disorders such as stroke due to a lack of blood supply to the brain or neurogenic shock resulting from loss of vasomotor tone is not necessarily

treated by administration of proliferating stem cell whereas other neurological conditions such as Alzheimer's disease are complex pathologies characterized by partial loss of myelin, axons, and oligodendroglial cells requiring treatment by targeting various processes.

Claims 18, 21, 32, 36, 38, 39, 40 and 41 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Horie et al., (US Patent 6,890,531, Date of Issue May 10, 2005) in view of Well et al., (Cell, 1991, pp. 91-97) and further in view of Johansson et al., (1999, Experimental cell research pp. 733-736).

Horie et al., teaches a method for treatment of neuropathy of **central nerves** caused by nerve injuries e.g., ischemia, infection, malignant tumor or metabolic disorder or degeneration of specific nerve system cells e.g., amyotrophic lateral sclerosis, diabetic neuropathy, dementia senilis, Alzheimer's disease, Parkinson's disease and the like are intractable (col. 2, lines 14-24; col. 13, lines 6-29). Moreover, Horie et al., teaches that galectin-1 is directly administrated to the site or galectin-1 is combined with a pharmaceutical carrier e.g., galectin-1 contained in collagen, to be directly imbedded into the neurological location for treatment (col. 5, lines 29-30, 40-41; col. 11, lines 60-61) (Current claims **18, 21, 32, in part)** . While Horie is silent as to cell proliferation induced by galectin-1 on neuronal stem cells on central nerve injury, administration of galectin-1 to central nerves must have inherently induced neuronal stem cells proliferation, since Horie has performed the same step of the claimed method, i.e., administration of galectin-1 to the brain. Note that the central nerve system includes the spinal cord level and brain level.

Horie et al., does not specifically disclose that Galactin-1 is involved in cell proliferation.

However, at the time the invention was made, Well et al., discloses a β galactoside-binding animal lectin, i.e., Galactin-1, which is expressed constitutively and operates in

regulation of cell proliferation (p. 96, col. 1, paragraph 1; Abstract) (Current claims **18, 21 and 32, in part**).

The combined references Horie and Well et al., fail to teach administration of Galectin-1 to the lateral ventricule of the brain.

However, at the time the invention was made, Johansson et al., discloses the two neurogenetic regions of the adult rodent brain: the wall of the lateral ventricule and the hippocampus (p. 733, col. 1). In addition, Johansson et al., teaches self-renewing cells from the adult human lateral ventricle wall and hippocampus capable of generating neurons, astrocytes and oligodendrocytes *in vitro*, contemplating the possibility of utilizing the potential neuronal production in the adult human brain to develop transplantation strategies or to stimulate neurogenesis *in situ* in the brain in neurodegenerative diseases (p. 733; col. 2; p. 736, col. 1) (**Current claims 36, 38-41, in part**).

Based on the combined teachings of Horie et al., of the treatment of cerebral ischemia and neural degenerative disease by administration of Galactin-1, and the teachings of Well et al., wherein Galactin-1 is involved in the regulation of cell proliferation, one of ordinary skill in the art would recognize that treatment of cerebral ischemia and neural degenerative disease by administration of Galactin-1 implicitly involves regeneration and remyelinization from central nerve injuries as well as regulation of cell proliferation. Additionally, one of ordinary skill would recognize that proliferation of neuronal stem cells, though no explicitly disclosed by the combined references, would be intrinsically necessary to the administration of Galactin-1 as Galactin-1 regulates constitutively cell division. Moreover, the recitation of the intended used in the claimed invention, namely, proliferation of neuronal stem cells, in the preamble of claims 18,

21, 32, and 36 fails to impart any physical or structural property to the method of administration, thus proliferation of neuronal stem cells would reasonably be expected as the combined reference of Horie and Wells clearly disclose the same steps i.e., administration of Galactin-1 resulting in treatment of the claimed neurological disorders and regulation of cell proliferation. Moreover, it would have been *prima facie* obvious for one of skill in the art, as a matter of design of choice to administer Galactin-1 to any brain region associate with the contemplated treatment of a neurological disorders including the wall of the lateral ventricule and the hippocampus in order to ameliorate said neurodegenerative disorder in a subject, particularly because Johansson et al., discloses these two neurogenetic regions of the adult rodent brain suitable to develop therapies for neurodenerative diseases. There would have been a reasonable expectation of success to use the methods of enhancing cell proliferation (e.g., neuronal stem cells) i*n vivo* by administration of Galactin-1 for the treatment of cerebral ischemia and neural degenerative disease as taught by Horie et al., Well et al., and Johansson given the results of the publications demonstrating the success of the methodologies, and materials detailed in each of the disclosures.

Other art for Comment

The following are cited to complete the record.

a) Vas V et al., Biphasic effect of recombinant galectin-1 on the growth and death of early hematopoietic cells. Stem Cells. 2005 Feb ;23(2):279-87.

Conclusion

Claims 18, 19, 21, 22, 27, 31-41 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of

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